Summary Basis of Approval
OB-NDA 98-0123

Product: Anticoagulant Sodium Citrate 4% w/v Solution, U.S.P. in Plastic Bag

Company: Haemonetics Corporation
400 Wood Road
Braintree, MA 02184

Date of Application: January 22, 1998

I. Indication for Use:
The product is for use only with automated apheresis devices in the collection of human plasma or in performing therapeutic plasma exchange procedures. The 4% Sodium Citrate is metered by the apheresis machine into the collected whole blood, the plasma is collected into a plasma collection bag and the cellular components are returned to the donor. The anticoagulant is not to be infused directly into the donor.

II. Dosage Form:
The 4% Sodium Citrate is used in an anticoagulant to whole blood ratio of 1:16. A flexible PVC plastic bag contains 250 mL of 4% Sodium Citrate and has a filling leg and a twist-off closure which accepts a spike from an apheresis collection set. The plastic bag is contained in an overwrap which is added prior to sterilization.

III. Manufacturing and Controls:

A. Manufacturing:
No new drug substance is involved in this NDA. The formulation for the 4% Sodium Citrate is in accordance with USP XXIII. The plastic bags are made by [redacted]. The anticoagulant solution is manufactured and filled into bags at the Haemonetics Corporation facility in Union, SC. Testing is performed on the environment, raw materials, in-process and finished products to assure that appropriate requirements and specifications are met.

B. Stability Studies:
Data was submitted on three lots of product held at room temperature and at 40°C for 6 months. [redacted]

C. Methods of Validation
All critical manufacturing steps, including sterilization and all systems have been successfully validated and are part of the NDA.

D. Labeling:
Draft labeling has been submitted. No trade name is being used. The Directions for Use are contained in the appropriate apheresis machine manual.

E. Establishment Inspection:
The Union, SC facility had a Pre-Approval Inspection for Dextrose 5% Injection, USP May 2 – 6, and June 29, 1994. The facility had a regularly scheduled inspection March 17 – 20, 1997.

F. Environmental Impact Statement:
4% Sodium Citrate solution is exempted per 21 CFR 25.24(c)(4).

IV. Pharmacokinetics and Bioavailability:
Since no new drug substance is involved in the 4% Sodium Citrate and the bag has been used extensively in Europe with this and other anticoagulants, no pharmacokinetic or bioavailability data are included.

V. Clinical Data:
During a meeting between Haemonetics and members of the CBER staff it was agreed that no clinical studies would be needed.

V. Safety and Efficacy:
Haemonetics has sold over ——— units of 4% Sodium Citrate with its name on the product since April, 1997. During that time no serious adverse reports have been received and no recalls of this 4% Sodium Citrate have been necessary. Reprints are included in the NDA to offer further proof of the safety and efficacy of 4% Sodium Citrate.

Betsy Pendleton 2.28.2000

2/29/2000